PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 717021	**FOR FURTHER ACTION**	See Form PCT/IPEA/416
International application No. **PCT/AU2004/000429**	International filing date *(day/month/year)* 2 April 2004	Priority date *(day/month/year)* 2 April 2003
International Patent Classification (IPC) or national classification and IPC **Int. Cl.** [7] G01N 33/52, G01N 33/574, C12Q 1/68		
Applicant ADELAIDE RESEARCH & INNOVATION PTY LTD et al		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 8 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. [X] *(sent to the applicant and to the International Bureau)* a total of **18** sheets, as follows:
      - [X] sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      - [ ] sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.

   b. [ ] *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or table related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).
4. This report contains indications relating to the following items:

[X]	Box No. I	Basis of the report
[ ]	Box No. II	Priority
[X]	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
[ ]	Box No. IV	Lack of unity of invention
[X]	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
[X]	Box No. VI	Certain documents cited
[ ]	Box No. VII	Certain defects in the international application
[X]	Box No. VIII	Certain observations on the international application

Date of submission of the demand 29 October 2004	Date of completion of the report 5 August 2005
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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/AU2004/000429

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language which is the language of a translation furnished for the purposes of:

   ☐ international search (under Rules 12.3 and 23.1 (b))

   ☐ publication of the international application (under Rule 12.4)

   ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements** of the international application, this report is based on (*replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report*):

   ☐ the international application as originally filed/furnished

   ☒ the description:

   pages **1-87** as originally filed/furnished
   pages* received by this Authority on with the letter of
   pages* received by this Authority on with the letter of

   ☒ the claims:

   pages as originally filed/furnished
   pages* as amended (together with any statement) under Article 19
   pages* **88-105** received by this Authority on 17.02.05 with the letter of 17.02.05
   pages* received by this Authority on with the letter of

   ☒ the drawings:

   pages **1/15-15/15** as originally filed/furnished
   pages* received by this Authority on with the letter of
   pages* received by this Authority on with the letter of

   ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

   ☐ the description, pages
   ☐ the claims, Nos.
   ☐ the drawings, sheets/figs
   ☐ the sequence listing (*specify*):
   ☐ any table(s) related to the sequence listing (*specify*):

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

   ☐ the description, pages
   ☐ the claims, Nos.
   ☐ the drawings, sheets/figs
   ☐ the sequence listing (*specify*):
   ☐ any table(s) related to the sequence listing (*specify*):

* *If item 4 applies, some or all of those sheets may be marked "superseded."*

Box No. III **Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application

☒ claims Nos: **59-103**

because:

☐ the said international application, or the said claims Nos.
relate to the following subject matter which does not require an international preliminary examination *(specify)*:

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos.
are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos.
are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claim Nos. **59-103**

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form
- ☐ has not been furnished
- ☐ does not comply with the standard

the computer readable form
- ☐ has not been furnished
- ☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See Supplemental Box for further details.

Box No. V **Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims **4-13, 16-20, 22, 28, 29, 33-42, 45-49, 51, 52, 54, 55, 57, 58, 104-124**	**YES**
	Claims **1-3, 14, 15, 21, 23-27, 30-32, 43, 44, 50, 53 and 56**	**NO**
Inventive step (IS)	Claims **NONE**	**YES**
	Claims **1-58, 104-124**	**NO**
Industrial applicability (IA)	Claims **1-58, 104-124**	**YES**
	Claims	**NO**

2. Citations and explanations (Rule 70.7)

The following documents identified in the International Search Report have been considered for the purposes of this report:

D1: Fiegler. H., *et al*; Genes Chromosomes Cancer (2003, April; published online 27.01.2003), 36 (4): 361-74.

D2: Martinez-Ramirez. A., *et al*; Cancer Genetics and Cytogenetics (2003), 144(1): 87-89.

D3: Sudbark. R., *et al*; Human Molecular Genetics (2001), 10(1): 77-83.

D4: Voullaire. L., *et al*; Prenatal Diagnosis (1999), 19 (9): 846-51.

D5: Solinas-Toldo. S., *et al*, Genes Chromosomes Cancer; (1997), 20 (4): 399-407.

D6: WO 2000/024925 (Luminis Pty Ltd) published 02.05.00.

D7: Hu. D. G., *et al*; Molecular Human Reproduction (2004), 10 (4): 283-9.

D8: WO 2003/027638 (spectral Genomics, Inc) published 03.04.2003.

The invention lies in a method for comparing chromosomes from two different cells of different karyotypes for detecting chromosomal abnormalities using CGH and micro arrays. The method involves the DOP-PCR amplification of a chromosome and the DNA from the cells of the two different karyotypes. The amplified DNA from the cells are labelled with different detectable labels and hybridised to the amplified chromosome that is attached to a solid surface. A comparison is then made of the hybridisation, by comparing the relative amount of label.

Continued in supplemental box

Box No. VI Certain documents cited

1. Certain published documents (Rule 70.10)

Application No. Patent No.	Publication date *(day/month/year)*	Filing date *(day/month/year)*	Priority date (valid claim) *(day/month/year)*
PX WO 2003/027638	3 April 2003	27 September 2002	27 September 2001

The document discloses all the essential features of claims 1-6, 11-16, 19-27, 29-35, 40-45 and 48-58 and therefore the claims are not novel. The citation was published before the filing date and after the priority date of the present application and therefore for the purposes of this opinion the citation is not relevant to novelty or inventive step of the claimed invention. However, should the validity of the present application's priority come into question, the citation may become relevant, or may also be relevant as a whole of contents citation under certain jurisdictions.

See the whole document.

2. Non-written disclosures (Rule 70.9)

Kind of non-written disclosure	Date of non-written disclosure *(day/month/year)*	Date of written disclosure referring to non-written disclosure *(day/month/year)*

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

Claims 59-103 are not fully supported by the specification. The invention lies in a method for comparing chromosomes from two different cells of different karyotypes for detecting chromosomal abnormalities using CGH and micro arrays. Claims 59-103, however, relate to a nucleic acid that is attached to a solid surface. The claims seem to lack what appears to be an essential feature of the invention- a method of detecting chromosomal abnormalities, and as such the claims are not fully supported by the description. Therefore in the absence of the claims being limited to the inventive concept of the invention claims 59-103 are not fully supported by the specification.

Supplemental Box V

In case the space in any of the preceding boxes is not sufficient.

Continuation of:

Novelty:

D1 teaches of a method of detecting chromosomal abnormalities. The method used to detect the abnormalities is the same as the one disclosed in the application, and involves the use of comparative genomic hybridisation (CGH) and micro arrays. The micro arrays were prepared using PAC and BAC clones, which are similar to that of the 'isolated chromosome of the invention (page7 lines 18 and 19). The clones were amplified using DOP-PCR primers and fixed on a solid surface to form the array. The reference and test DNAs were also amplified using DOP-PCR and labelled with different labels -Cy5 and Cy3 (page 364, col 2, last para) and then hybridised to the array and the signals compared to detect chromosomal abnormalities. As such, the citation discloses all the essential features of claims 1-3, 14, 15, 21, 23-27, 30-32, 43, 44, 50, 53 and 56 therefore the invention is not novel.

D7 discloses all the essential features of claims 1-3, 5-15, 17-32, 34-44 and 46-58. The citation discloses methods of detecting aneuploidy and genetic mosaicism using CGH and micro arrays. The citation was published after the priority date and therefore cannot be used as a novelty or inventive step citation. However, should the validity of the present application's priority come into question, the citation may become relevant.

D8 may be relevant for novelty under certain jurisdictions, see Box VI.

Inventive Step:

The problem addressed by the current application is a method for comparing chromosomes from two different cells of different karyotypes for detecting chromosomal abnormalities using CGH and micro arrays. The citations D1-D6 are directed towards a similar problem. In searching the art a diligent searcher investigating this problem could reasonably be expected to have found these documents. Further it would have been obvious to the skilled worker to combine the documents to arrive at a solution which is the same as the claimed solution.

Claims 1-6, 11-16, 19-35, 40-45, 48-58 and 104-124 lack an inventive step in light of each of D2-D4 and D6 in combination with D1. As indicated in the following paragraphs D2-D4 and D6 each individually disclose various methods of detecting abnormalities in chromosomes using CGH in combination with micro arrays, what seems to be lacking in these citations is the amplification of all the DNA/chromosomes involved. D1 teaches of the DOP-PCR amplification of these molecules. As such it would be obvious to the PSA to combine the citations in order to amplify small amounts of DNA/chromosome (that may be obtained, for example, from a single cell) and then use the combined technique of CGH and micro arrays to detect chromosomal abnormalities. Therefore in light of the combined citations claims 1-6, 11-16, 19-35, 40-45, 48-58 and 104-124 lack an inventive step.

D1 discloses most of the essential features of the invention. However, certain aspects that are not disclosed include:
-a specific DOP primer as disclosed in claims 4, 16, 33 and 45
-the size of the chromosome that is amplified, and
-the number of cells from which the first and second karyotype DNA are amplified.
However, these differences between the citation and the invention lies within the bounds of what is well known in the art and it would clearly have been obvious to the person skilled in the art (PSA) that any one of these parameters could be replaced by the other without materially affecting the way the invention worked. The PSA would directly and without difficulty, by routine steps, have produced the claimed invention. Therefore, in the absence of suggestion of practical difficulties overcome or unexpected features associated with the invention claims 4-6, 11-13, 16, 19, 20, 22, 33-35, 40-42, 45, 48, 49, 51, 52, 54 and 55 disclose nothing more than routine application of standard steps and techniques and therefore the claims lack an inventive step in light of D1 in combination with each of D2-D4 and D6.

Continued in supplemental box

Supplemental Box V

In case the space in any of the preceding boxes is not sufficient.

Continuation of Inventive Step:

Citation D2 discloses a combination of CGH and micro arrays to screen for amplification and deletion in tumour genomes. The citation does not disclose the amplification of either the isolated chromosome or the first and second karyotype DNAs, however, the amplification of small quantities of DNA using DOP-PCR is well known in the art (D1, D4, D6) and it would be obvious for the PSA to use this technique to get larger quantities of DNA. As such, claims 1, 6, 11-13, 21, 22, 27-30 are not inventive in light of this citation in combination with D1.

D3 also uses a similar technique of micro arrays of human X-chromosomes. Reference and normal male and female chromosomes were labelled with Cy5 and Cy3 respectively and cohybridised on the micro arrays. Claims 1, 5, 6, 11-14, 19-30, 34-43, 48-58 and 104-124 are not inventive in light of this citation in combination with D1.

D4 discloses a method of detecting aneuploidy in a single cell using CGH and DOP-PCR. The test and reference samples are amplified using DOP-PCR and labelled with Spectrum Red and Spectrum Green labels. The difference between citation and the invention is that the chromosomal DNA is not amplified, therefore claims 1-6, 11-36, 40-45, 48-58 and 104-124 are not inventive in light of this citation in combination with D1.

D6 is a method of comparing chromosomes of unknown karyotype with a corresponding known chromosome. The citation teaches of using the technique for preimplantation diagnosis from a single cell. The only difference between the citation and the invention is the lack of amplification of a single chromosome to form the array. However, as pointed out earlier there is not inventive step involved in the DOP-PCR amplification of the chromosome. Therefore claims 1-6, 11-16, 19-35, 40-45, 48-58 and 104-124 are not inventive in light of this citation in combination with D1.

As such, claims 1-6, 11-16, 19-35, 40-45, 48-58 and 104-124 lack an inventive step in light of each of D2-D4 and D6 in combination with D1.

Claims:

1. A method of comparing at least one chromosome or part thereof from a cell with a first karyotype with the corresponding chromosome or part thereof from a cell with a second karyotype, the method including the steps of:

(a) amplifying DNA from an isolated chromosome or part of an isolated chromosome;

(b) attaching the amplified DNA to a solid substrate;

(c) amplifying DNA from one or more cells with a first karyotype and amplifying DNA from one or more cells with a second karyotype;

(d) labelling the amplified DNA from the one or more cells with a first karyotype with a first label, and labelling the amplified DNA from the one or more cells with a second karyotype with a second label, wherein the first and second labels are detectably different;

(e) hybridizing the amplified and labelled DNA from the one or more cells with a first karyotype to the amplified DNA attached to the solid substrate, and hybridizing the amplified and labelled DNA from the one or more cells with a second karyotype to the amplified DNA attached to the solid substrate; and

(f) comparing the relative amount of first and second labels hybridized to the amplified DNA attached to the solid substrate.

2. A method according to claim 1, wherein the amplifying DNA from an isolated chromosome or a part of an isolated chromosome is randomly primed amplification.

3. A method according to claim 2, wherein the randomly primed amplification includes the use of a degenerate oligonucleotide primer.

4. A method according to claim 3, wherein the degenerate oligonucleotide primer consists of the nucleotide sequence 5'-CCGACTCGAGNNNNNNATGTGG-3', N being any nucleotide.

5. A method according to any one of claims 1 to 4, wherein the isolated chromosome is a chromosome isolated by microdissection or flow cytometry.

6. A method according to any one of claims 1 to 4, wherein the part of an isolated chromosome is a cloned fragment of a chromosome.

7. A method according to claim 6, wherein the amplified DNA from a part of an isolated chromosome is depleted of non-chromosomal sequences.

8. A method according to any one of claims 1 to 7, wherein the amplified DNA from an isolated chromosome or part of an isolated chromosome is depleted of repetitive sequences and/or sequences that over represented due to the amplifying of the DNA.

9. A method according to claim 8, wherein the amplified DNA from an isolated chromosome or part of an isolated chromosome is depleted of repetitive sequences.

10. A method according to claim 9, wherein the repetitive sequences include Cot-1 sequences, simple repeated DNA, satellite repeats, mini-satellite repeats, chromosome-specific repeats, micro-satellite repeats, repeated genes, sequences derived from transposable elements, elements derived from multiple copies of viruses such as retroviruses, repeats associated with centromeres or telomeres, and repeats associated with heterochromatin.

11. A method according to any one of claims 1 to 10, wherein the amplified DNA from an isolated chromosome or part of an isolated chromosome is size selected prior to attaching the amplified DNA to the solid substrate.

12. A method according to claim 11, wherein the amplified DNA from an isolated chromosome or part of an isolated chromosome is size selected for DNA of a size of less than 10 kb.

13. A method according to claim 11, wherein the amplified DNA from the isolated chromosome or part of an isolated chromosome is size selected for DNA of a size of less than 3 kb.

14. A method according to any one of claims 1 to 13, wherein the amplifying of DNA from one or more cells with a first karyotype and the amplifying of DNA from one or more cells with a second karyotype is randomly primed amplification.

15. A method according to claim 14, wherein the randomly primed amplification includes the use of a degenerate oligonucleotide primer.

16. A method according to claim 15, wherein the degenerate oligonucleotide primer consists of the nucleotide sequence 5'-CCGACTCGAGNNNNNNATGTGG-3', N being any nucleotide.

17. A method according to any one of claims 1 to 16, wherein the amplified DNA from one or more cells with a first karyotype and the amplified DNA from one or more cells with a second karyotype are both depleted of repetitive sequences.

18. A method according to claim 17, wherein the repetitive sequences are Cot-1 sequences.

19. A method according to any one of claims 1 to 18, wherein the amplified DNA from one or more cells with a first karyotype is DNA amplified from 1 to 20 cells.

20. A method according to any one of claims 1 to 18, wherein the amplified DNA from one or more cell with a first karyotype is DNA amplified from a single cell.

21. A method according to any one of claims 1 to 19, wherein the one or more cells with a first karyotype is an embryonic cell, a foetal cell, a germ cell, a cancerous cell, or a polar body.

22. A method according to claim 20, wherein the single cell is an embryonic cell, an oocyte, or a polar body.

23. A method according to any one of claims 1 to 22, wherein the one or more cells with a second karyotype is a cell of the same type as the one or more cells with a first karyotype.

24. A method according to any one of claims 1 to 23, wherein the amplified DNA from one or more cells with a second karyotype is DNA amplified from the same number of cells as the one or more cells with a first karyotype.

25. A method according to any one of claims 1 to 24, wherein the amplification of DNA from the isolated chromosome or part of the isolated chromosome further includes amplification of a specific chromosomal region.

26. A method according to any one of claims 1 to 25, wherein the amplification of DNA from one or more cells with a first karyotype and the amplification of DNA from one or more cells with a second karyotype further includes amplification of the same specific chromosomal region.

27. A method according to any one of claims 1 to 26, wherein the first label is Cy3-dUTP and the second label is Cy5-dUTP.

28. A method according to any one of claims 1 to 27, wherein the method is used for pre-implantation diagnosis of an embryo or an oocyte.

29. A method according to any one of claims 1 to 27, wherein the method is used for the prenatal diagnosis of a foetus for a chromosomal abnormality.

30. A method of detecting a chromosomal abnormality in a cell with an unknown karyotype, the method including the steps of:

(a) amplifying DNA from an isolated chromosome or part of an isolated chromosome;

(b) attaching the amplified DNA to a solid substrate;

(c) amplifying DNA from one or more cells with an unknown karyotype and amplifying DNA from one or more cells with a reference karyotype;

(d) labelling the amplified DNA from one or more cells with the unknown karyotype with a first label, and labelling the amplified DNA from one or more cells with the reference karyotype with a second label, wherein the first and second labels are detectably different;

(e) hybridising the amplified and labelled DNA from the one or more cells with an unknown karyotype to the amplified DNA attached to the solid substrate, and hybridising the amplified and labelled DNA from the one or more cells with a reference karyotype to the amplified DNA attached to the solid substrate; and

(f) detecting the presence of a chromosome abnormality in the cell with the unknown karyotype by comparing the relative amount of the first label hybridised to the amplified DNA attached to the solid substrate to the amount of a second label hybridised to the amplified DNA attached to the solid substrate.

31. A method according to claim 30, wherein the amplifying DNA from an isolated chromosome or a part of an isolated chromosome is randomly primed amplification.

32. A method according to claim 31, wherein the randomly primed amplification includes the use of a degenerate oligonucleotide primer.

33. A method according to claim 32, wherein the degenerate oligonucleotide primer consists of the nucleotide sequence 5'-CCGACTCGAGNNNNNNATGTGG-3', N being any nucleotide.

34. A method according to any one of claims 30 to 33, wherein the isolated chromosome is a chromosome isolated by microdissection or flow cytometry.

35. A method according to any one of claims 30 to 33, wherein the part of an isolated chromosome is a cloned fragment of a chromosome.

36. A method according to claim 35, wherein the amplified DNA from a part of an isolated chromosome is depleted of non-chromosomal sequences.

37. A method according to any one of claims 30 to 36, wherein the amplified DNA from an isolated chromosome or part of an isolated chromosome is depleted of repetitive sequences and/or sequences that over represented due to the amplifying of the DNA.

38. A method according to claim 37, wherein the amplified DNA from an isolated chromosome or part of an isolated chromosome is depleted of repetitive sequences.

39. A method according to claim 38, wherein the repetitive sequences include Cot-1 sequences, simple repeated DNA, satellite repeats, mini-satellite repeats, chromosome-specific repeats, micro-satellite repeats, repeated genes, sequences derived from transposable elements, elements derived from multiple copies of viruses such as retroviruses, repeats associated with centromeres or telomeres, and repeats associated with heterochromatin.

40. A method according to any one of claims 30 to 39, wherein the amplified DNA from an isolated chromosome or part of an isolated chromosome is size selected prior to attaching the amplified DNA to the solid substrate.

41. A method according to claim 40, wherein the amplified DNA from an isolated chromosome or part of an isolated chromosome is size selected for DNA of a size of less than 10 kb.

42. A method according to claim 40, wherein the amplified DNA from the isolated chromosome or part of an isolated chromosome is size selected for DNA of a size of less than 3 kb.

43. A method according to any one of claims 30 to 42, wherein the amplifying of DNA from one or more cells with an unknown karyotype and the amplifying of DNA from one or more cells with a reference karyotype is randomly primed DNA amplification.

44. A method according to claim 43, wherein the amplifying includes the use of a degenerate oligonucleotide primer.

45. A method according to claim 44, wherein the degenerate oligonucleotide primer consists of the nucleotide sequence 5'-CCGACTCGAGNNNNNNATGTGG-3', N being any nucleotide.

46. A method according to any one of claims 30 to 45, wherein the amplified DNA from one or more cells with an unknown karyotype and the amplified DNA from one or more cells with a reference karyotype are both depleted of repetitive sequences.

47. A method according to claim 46, wherein the repetitive sequences are Cot-1 sequences.

48. A method according to any one of claims 30 to 47, wherein the amplified DNA from one or more cells with an unknown karyotype is DNA amplified from 1 to 20 cells.

49. A method according to any one of claims 30 to 47, wherein the amplified DNA from one or more cells with an unknown karyotype is DNA amplified from a single cell.

50. A method according to any one of claims 30 to 48, wherein the one or more cells with an unknown karyotype is an embryonic cell, a foetal cell, a germ cell, a cancerous cell, or a polar body.

51. A method according to claim 50, wherein the single cell is an embryonic cell, an oocyte, or a polar body.

52. A method according to any one of claims 30 to 51, wherein the one or more cells with a reference karyotype is a cell of the same type as the one or more cells with an unknown karyotype.

53. A method according to any one of claims 30 to 52, wherein the amplified DNA from the one or more cells with a reference karyotype is DNA amplified from the same number of cells as the one or more cells with an unknown karyotype.

54. A method according to any one of claims 30 to 53, wherein the amplification of DNA from an isolated chromosome or a part of an isolated chromosome further includes amplification of a specific chromosomal region.

55. A method according to any one of claims 30 to 54, wherein the amplification of DNA from one or more cells with an unknown karyotype and the amplification of DNA from one or more cells with a reference karyotype further includes amplification of the same specific chromosomal region.

56. A method according to any one of claims 30 to 55, wherein the first label is Cy3-dUTP and the second label is Cy5-dUTP.

57. A method according to any one of claims 30 to 56, wherein the method is used for pre-implantation diagnosis of an embryo or an oocyte.

58. A method according to any one of claims 30 to 56, wherein the method is used for the prenatal diagnosis of a foetus for a chromosomal abnormality.

59. A nucleic acid attached to a solid substrate, wherein the nucleic acid is derived from an isolated chromosome or part of an isolated chromosome and the nucleic acid is depleted of repetitive sequences.

60. A nucleic acid according to claim 59, wherein the nucleic acid is derived from amplification of an isolated chromosome or part of an isolated chromosome.

61. A nucleic acid according to claim 60, wherein the amplification from an isolated chromosome or a part of an isolated chromosome is randomly primed amplification.

62. A nucleic acid according to claim 61, wherein the amplification from an isolated chromosome or a part of an isolated chromosome includes the use of a degenerate oligonucleotide primer.

63. A nucleic acid according to claim 62, wherein the degenerate oligonucleotide primer consists of the sequence 5'-CCGACTCGAGNNNNNNATGTGG-3', N being any nucleotide.

64. A nucleic acid according to any one of claims 59 to 63, wherein the isolated chromosome is a chromosome isolated by microdissection or flow cytometry.

65. A nucleic acid according to any one of claims 59 to 63, wherein the part of an isolated chromosome is part of a chromosome isolated by microdissection or flow cytometry.

66. A nucleic acid according to any one of claims 59 to 63, wherein the part of an isolated chromosome is a cloned fragment of a chromosome.

67. A nucleic acid according to claim 66, wherein the nucleic acid is also depleted of non-chromosomal sequences.

68. A nucleic acid according to any one of claims 60 to 67, wherein the amplified DNA from an isolated chromosome or part of an isolated chromosome is also depleted of sequences that are over represented due to amplification.

69. A nucleic acid according to any one of claims 59 to 68, wherein the repetitive sequences include Cot-1 sequences, simple repeated DNA, satellite repeats, mini-satellite repeats, chromosome-specific repeats, micro-satellite repeats, repeated genes, sequences derived from transposable elements, elements derived from multiple copies of viruses such as retroviruses, repeats associated with centromeres or telomeres, and repeats associated with heterochromatin.

70. A nucleic acid according to any one of claims 59 to 69, wherein the amplified nucleic acid from an isolated chromosome or part of an isolated chromosome is size selected.

71. A nucleic acid according to claim 70, wherein the amplified nucleic acid from an isolated chromosome or part of an isolated chromosome is size selected for a size of less than 10 kb.

72. A nucleic acid according to claim 70, wherein the amplified nucleic acid from the isolated chromosome or part of an isolated chromosome is size selected for a size of less than 3 kb.

73. A nucleic acid according to any one of claims 59 to 72, wherein the nucleic acid attached to the substrate is a target for hybridization.

74. A nucleic acid according to claim 73, wherein the nucleic acid attached to the substrate is a target for comparative genomic hybridisation.

75. An array of nucleic acids, the array including one or more nucleic acids attached to a solid substrate according to any one of claims 59 to 74.

76. A nucleic acid attached to a solid substrate, wherein the nucleic acid is derived from randomly primed amplification of an isolated chromosome or part of an isolated chromosome, and the nucleic acid is depleted of one or more of repetitive sequences, non-chromosomal sequence or sequences that are over-represented due to the amplification.

77. A nucleic acid according to claim 76, wherein the randomly primed amplification includes the use of a degenerate oligonucleotide primer.

78. A nucleic acid according to claim 77, wherein the degenerate oligonucleotide primer consists of the nucleotide sequence 5'-CCGACTCGAGNNNNNNATGTGG-3', N being any nucleotide.

79. A nucleic acid according to any one of claims 76 to 78, wherein the isolated chromosome is an chromosome isolated by microdissection or flow cytometry.

80. A nucleic acid according to any one of claims 76 to 78, wherein the part of an isolated chromosome is a part of a chromosome isolated by microdissection or flow cytometry.

81. A nucleic acid according to any one of claims 76 to 78, wherein the part of an isolated chromosome is a cloned fragment of a chromosome.

82. A nucleic acid according to any one of claims 76 to 81, wherein the repetitive sequences include Cot-1 sequences, simple repeated DNA, satellite repeats, mini-satellite repeats, chromosome-specific repeats, micro-satellite repeats, repeated genes, sequences derived from transposable elements, elements derived from multiple copies of viruses such as retroviruses, repeats associated with centromeres or telomeres, and repeats associated with heterochromatin.

83. A nucleic acid according to any one of claims 76 to 82, wherein the non-chromosomal sequences are bacterial sequences.

84. A nucleic acid according to any one of claims 76 to 83, wherein the amplified nucleic acid from the isolated chromosome or part of an isolated chromosome is size selected.

85. A nucleic acid according to claim 84, wherein the amplified nucleic acid from an isolated chromosome or part of an isolated chromosome is size selected for a size of less than 10 kb.

86. A nucleic acid according to claim 84, wherein the amplified nucleic acid from the isolated chromosome or part of an isolated chromosome is size selected for a size of less than 3 kb.

87. A nucleic acid according to any one of claims 76 to 86, wherein the nucleic acid attached to the solid substrate is a target for hybridisation.

88. A nucleic acid according to claim 87, wherein the nucleic acid attached to the solid substrate is a target for comparative genomic hybridisation.

89. An array of nucleic acids attached to a solid substrate, the array including one or more nucleic acids attached to a solid substrate according to any one of claims 76 to 88.

90. A nucleic acid derived from randomly primed amplification of an isolated chromosome or part of an isolated chromosome, wherein the nucleic acid is depleted of repetitive sequences.

91. A nucleic acid according to claim 90, wherein the randomly primed amplification includes the use of a degenerate oligonucleotide primer.

92. A nucleic acid according to claim 91, wherein the degenerate oligonucleotide primer consists of the nucleotide sequence 5'-CCGACTCGAGNNNNNNATGTGG-3', N being any nucleotide.

93. A nucleic acid according to any one of claims 90 to 92, wherein the isolated chromosome is isolated by microdissection or flow cytometry.

94. A nucleic acid according to any one of claims 90 to 92, wherein the part of an isolated chromosome is part of a chromosome isolated by microdissection or flow cytometry.

95. A nucleic acid according to any one of claims 90 to 92, wherein the part of an isolated chromosome is a cloned fragment of a chromosome.

96. A nucleic acid according to claim 95, wherein the nucleic acid is also depleted of non-chromosomal sequences.

97. A nucleic acid according to any one of claims 91 to 96, wherein the nucleic acid is further depleted of sequences that are over represented due to amplification.

98. A nucleic acid according to any one of claims 90 to 97, wherein the repetitive sequences include Cot-1 sequences, simple repeated DNA, satellite repeats, mini-satellite repeats, chromosome-specific repeats, micro-satellite repeats, repeated genes, sequences derived from transposable elements, elements derived from multiple copies of viruses such as retroviruses, repeats associated with centromeres or telomeres, and repeats associated with heterochromatin.

99. A nucleic acid according to any one of claims 90 to 98, wherein the nucleic acid is size selected.

100. A nucleic acid according to claim 99, wherein the nucleic acid is size selected for a size of less than 10 kb.

101. A nucleic acid according to claim 88, wherein the nucleic acid is size selected for a size of less than 3 kb.

102. A nucleic acid according to any one of claims 90 to 101, wherein the nucleic acid is a target nucleic acid for hybridisation.

103. A nucleic acid according to claim 102, wherein the nucleic acid is a target nucleic acid for comparative genomic hybridisation.

104. A method of comparing at least one chromosome or part thereof from a cell with a first karyotype with the corresponding chromosome or part thereof from a cell with a second karyotype, the method including the steps of:

(a) randomly amplifying DNA from an isolated chromosome or part of an isolated chromosome, the amplified DNA being depleted of repetitive sequences and/or sequences that are over represented due to the random amplification;

(b) attaching the amplified DNA to a solid substrate;

(c) amplifying DNA from one or more cells with a first karyotype and amplifying DNA from one or more cells with a second karyotype;

(d) labelling the amplified DNA from the one or more cells with a first karyotype with a first label, and labelling the amplified DNA from the one or more cells with a second karyotype with a second label, wherein the first and second labels are detectably different;

(e) hybridizing the amplified and labelled DNA from the one or more cells with a first karyotype to the amplified DNA attached to the solid substrate, and hybridizing the amplified and labelled DNA from the one or more cells with a second karyotype to the amplified DNA attached to the solid substrate; and

(f) comparing the relative amount of first and second labels hybridized to the amplified DNA attached to the solid substrate.

105. A method according to claim 104, wherein the method is used for the detection of a chromosomal abnormality in the cell with a first karyotype.

106. A method according to claims 104 or 105, wherein the method is used for pre-implantation diagnosis of an embryo or an oocyte.

107. A method according to claims 104 or 105, wherein the method is used for the prenatal diagnosis of a foetus.

108. A method according to claims 104 or 105, wherein the method is used for the determination of karyotype of cancerous cells.

109. A method of detecting a chromosomal abnormality in a cell with an unknown karyotype, the method including the steps of:

(a) randomly amplifying DNA from an isolated chromosome or part of an isolated chromosome, the amplified DNA being depleted of repetitive sequences and/or sequences that are over represented due to the random amplification;

(b) attaching the amplified DNA to a solid substrate;

(c) amplifying DNA from one or more cells with an unknown karyotype and amplifying DNA from one or more cells with a reference karyotype;

(d) labelling the amplified DNA from the one or more cells with an unknown karyotype with a first label, and labelling the amplified DNA from one or more cells with a reference karyotype with a second label, wherein the first and second labels are detectably different;

(e) hybridising the amplified and labelled DNA from the one or more cells with an unknown karyotype to the amplified DNA attached to the solid substrate, and hybridising the amplified and labelled DNA from the one or more cells with a reference karyotype to the amplified DNA attached to the solid substrate; and

(f) detecting the presence of a chromosome abnormality in the cell with the unknown karyotype by comparing the relative amount of the first label hybridised to the amplified DNA attached to the solid substrate to the amount of a second label hybridised to the amplified DNA attached to the solid substrate.

110. A method according to claim 109, wherein the method is used for pre-implantation diagnosis of an embryo or an oocyte.

111. A method according to claim 109, wherein the method is used for the prenatal diagnosis of a foetus.

112. A method according to claim 109, wherein the method is used for the determination of karyotype of a cancerous cell.

113. A method of comparing at least one chromosome or part thereof from a cell with a first karyotype with the corresponding chromosome or part thereof from a cell with a second karyotype, the method including the steps of:

(a) randomly amplifying DNA from an isolated chromosome or part of an isolated chromosome;

(b) attaching the amplified DNA to a solid substrate;

(c) randomly amplifying DNA from 100 or less cells with a first karyotype and randomly amplifying DNA from one or more cells with a second karyotype;

(d) labelling the randomly amplified DNA from the cells with a first karyotype with a first label, and labelling the randomly amplified DNA from the one or more cells with a second karyotype with a second label, wherein the first and second labels are detectably different;

(e) hybridising the amplified and labelled DNA from the cells with a first karyotype to the amplified DNA attached to the solid substrate, and hybridising the amplified and labelled DNA from the one or more cells with a second karyotype to the amplified DNA attached to the solid substrate; and

(f) comparing the relative amount of first and second labels hybridised to the amplified DNA attached to the solid substrate.

114. A method according to claim 113, wherein the random amplification of DNA from the cells with a first karyotype is random amplification of DNA from 1 to 20 cells.

115. A method according to claims 113 or 114, wherein the random amplification of DNA from the cells with a first karyotype is direct amplification of DNA extracted from the cells.

116. A method according to any one of claims 113 to 115, wherein lysis of the cells with a first karyotype and the random amplification of DNA resulting from the lysis occur in the same tube.

117. A method according to any one of claims 113 to 116, wherein the random amplification of DNA from the cells with a first karyotype is amplification of substantially the entire DNA extracted from the one or more cells with a first karyotype.

118. A method according to any one of claims 113 to 117, wherein the method includes the step of performing a further round of random amplification of the DNA randomly amplified from the cells with a first karyotype and the labelling of the DNA with a first label occurs concurrently with and/or after the further round of random amplification.

119. A method according to any one of claims 113 to 118, wherein the randomly amplified DNA from the cells with the first karyotype and/or the randomly amplified DNA from the cells with the second karyotype is depleted of Cot-1 sequences, the depletion of the Cot-1 sequences including the use of randomly amplified Cot-1 DNA.

120. A method according to any one of claims 113 to 119, wherein the cells with a first karyotype are washed before the random amplification.

121. A method according to any one of claims 113 to 120, wherein the method is used for the detection of a chromosomal abnormality in the cell with a first karyotype.

122. A method according to any one of claims 113 to 121, wherein the method is used for pre-implantation diagnosis of an embryo or an oocyte.

123. A method according to any one of claims 113 to 121, wherein the method is used for the prenatal diagnosis of a foetus.

124. A method according to any one of claims 113 to 121, wherein the method is used for the determination of karyotype of a cancerous cell.